Simulation of Human Cardiovascular System

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by

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Abstract

In traditional pulse diagnosis method which was highly popular in India and China, many diseases of internal organs like heart, intestine, liver, etc. are diagnosed by measuring the blood pulse by palpating using three fingers placed on the radial artery just below the wrist. The diagnosis is made by inferring the qualitative features of the pressure pulses under these three fingers. Though efficient, the diagnosis can only be done by highly experienced practitioners who are few in number. A solution to this problem would be to develop a measurement system with which the pulses can be measured accurately and diagnosis can be done objectively. Developing such a system demands knowledge of how the pulse diagnosis works in terms of the physiology of human body.

Blood pulse is a pressure wave of distension caused by the pumping of heart. It is part of the human cardiovascular system. Since a mathematical model can be used to gain deeper insights about the system, a reasonably accurate model of the cardiovascular system would be helpful in analysing the pressure pulse waveforms produced at the radial artery. Once a model is available it can be simulated in an appropriate platform and the pulses can be analysed closely which would obviate the necessity of measuring it from real subjects. This would help to shed light into the science behind the methodology of pulse diagnosis.

In this work, a model of the cardiovascular system is sought with which the manifestation of pulses at the radial artery can be studied. The cardiovascular models by M. Ursino and Leaning *et al.* is studied in detail. The left ventricular and aortic pressure waveforms generated using the former model was similar to the waveforms measured in vivo. The model by Leaning *et al.* gives an elaborate representation of the vascular system and also considers the gravitational effects on the orientation of the vessels. To exploit the advantages of both models, they are combined into a single model. The model is simulated in Simulink and the pressure waveforms at the left ventricle, aorta and arm are generated. The simulated waveform is qualitatively similar to the pressure waveform. With further investigation an accurate model of the cardiovascular system which can generate the three pulses at the radial artery can be developed.

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First and foremost I am deeply grateful to my supervisor, Dr. Supratim Gupta, for the timely and accurate guidance he has provided me. This thesis was made possible by following his suggestions and directions. And special thanks to him for inspiring me and for instilling in me the necessary attitude and skills necessary for a research career.

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Sajith Kumar K K

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ABBREVIATIONS

RA	**R**ight **A**trium
LA	**L**eft **A**trium
RV	**R**ight **V**entricle
LV	**L**eft **V**entricle
SA	**S**ino **A**trial
AV	**A**trio **V**entricular
SV	**S**troke **V**olume
CO	**C**ardiac **O**utput
HR	**H**eart **R**ate
RBC	**R**ed **B**lood **C**ells
WBC	**W**hite **B**lood **C**ells
EDV	**E**nd **D**iastolic **V**olume
ESV	**E**nd **S**ystolic **V**olume
CVS	**C**ardio **V**ascular **S**ystem

PHYSICAL CONSTANTS

$$\text{Acceleration due to gravity} \quad g = 9.8m/s^2$$

SYMBOLS

P	Pressure	mmHg
F	Volumetric Flow Rate	m^3/s
R	Flow Resistance	mmH.s/m^3
r	Radius	m
L	Lenght	m
η	Viscocity	mmHg.s
C	Compliance	m^3/mmHg
ρ	Density	m^3/kg
A	Area	m^2
V	Volume	m^3
t	Time	s
ϕ	Angle	deg

Dedicated to my nephew, Devak

CHAPTER 1

INTRODUCTION

1.1 Introduction

In present day one visits a medical doctor to diagnose his illness. Many technological methods or aids are used for probing and determining a disease. Magnetic Resonance Imaging, X-Ray, Computer Tomography, endoscopy, ultrasonic are some of the technological methods. Besides, different medical tests like blood test are also used by the doctor in finding out the disease. Doctors also rely on external symptoms visible in the body that may indicate the presence of an ailment in the body.

In ancient civilizations medical practitioners relied on non-invasive techniques for diagnosis. Pulse-diagnosis is one such method in which the practitioner reads the physiological state by measuring the blood pulse. The art of diagnosing diseases from blood pulse is known as pulse science or sphygmology. This science was extensively developed in Traditional Chinese Medicine and Indian Ayurvedic System[1]. Egyptian, Greek and Arabic civilizations also used pulse diagnosis, though they were not as extensive as it was in India and China. In all these civilizations, the medical practitioners used to diagnose the patients by just qualitatively measuring the blood pulse in the radial artery. Unlike the modern clinician who measures a single pulse, they measured three distinct pulses at the wrist. In Ayurvedic literature these three pulses are termed as Vata, Pitta and Kapha pulses. They correspond to the lower, middle and upper part of the human body respectively.

The pulse diagnosis method known as Nadipariksha was highly popularised in India during the medieval period[1]. For effective diagnosis using this technique, the practitioner has to be very experienced and capable. The measurement is qualitative and depends on the concentration, focus and previous experience of the partitioner. This has limited the number of practitioners who can perform a reliable and accurate diagnosis to a handful. And with the advent of modern medicine, this method came to be used lesser and lesser. Nevertheless, a highly experienced one can diagnose a wide variety of diseases to a high degree of accuracy. Padmabhushan Pandit Satya Narayan Shastri of Varanasi was a renowned expert in Nadiparisha in recent years[1].

The fact that practitioners find diseases about internal organs from radial pulse alone indicates that there is rich physiological information in the radial pulse. Scientifically validating this through the physiology of human body would be a good step towards substantiating the Ayurvedic approach of diagnosis.

Mathematical models are extremely useful tools in providing deeper insights about a system. They tell heaps about how a system behave in different conditions. One important advantage of a model is that it helps in testing theories about a system. Model of the human cardiovascular system, in which the blood pulse manifests, would be helpful in understanding the system in depth. In this thesis, a better mathematical model for representation of the human cardiovascular system is sought so that a three pulse diagnosis method can be validated. The model is simulated in Simulink.

1.2 Motivation

The pulse-diagnosis method is an ancient method which is not that popular in the present days. Also, there is no scientific explanation on how the diseases are found from pulse information. Due to this, there is a general disbelief in the methodology. However, a subjective experience of being diagnosed by the method changes the perception towards it. My supervisor's belief in the method was consolidated when he had such an experience. An Ayurvedic practioner diagnosed an ucler in his duodenum by solely palpating his wrist with three fingers for some time. Though the enodscopy result which confirmed the abnormality was there with him, the practitoner was unaware of it. This surprised my supervisor since the practioner used only pulse information to precisely point where the ulcer is located, and motivated him to do research related to pulse science.

Reviewing the literature on pulse science, it is seen that physiological information about heart, liver, kidney, intestines, gall bladder and stomach can be obtained from measurement of pulses at the radial artery alone. A logical inference of this would be that the physiological information of human body is reflected in these three pulses in the radial artery. No matter what conceptual scheme the practitioners use, there should be a physical manifestation of the same. To scientifically validate the methodology, it has to be understood in terms of the physiology of the human body.

One major problem with this methodology is that only a highly experienced Ayurvedic practitioner can diagnose diseases with high level of accuracy and reliability. The learning curve is quite steep and a high level of commitment and dedication is required to master the method. Hence only few practitioners are there who are good at it. A natural concern is that within the next few generations the rich knowledge of Nadipariksha(pulse diagnosis) could gradually become extinct. A solution to this problem would be to develop a digital device which can perform the diagnosis objectively without the help of a practitioner. This would help in eliminating subjective errors as well. The development of such a system demands understanding how the diagnosing is done in terms of the underlying human physiology.

Blood pulse is a pressure wave of distension caused by the pumping of heart. It is part of an organ system: the human cardiovascular system, which is comprised of heart, blood and blood vessels. A mathematical model can be used to gain deeper insights about the system. Also it can be used to test different hypotheses about the system. A reasonably accurate model of the cardiovascular system would be helpful in analysing the pressure pulse waveforms produced at the radial artery. Such a model can be simulated in an appropriate platform and the pulses at the radial artery can be analysed closely which would obviate the necessity of measuring it from real subjects.

In this work an appropriate model of the human cardiovascular system is sought and the pressure waveforms at arm are simulated in Simulink.

1.3 Objective

To develop a model of the cardiovascular system with which the three distinct pressure pulse waveforms at the radial artery can be simulated.

1.4 Thesis Organization

This thesis is organized as follows:

- **Chapter 2:** Literature review on ancient pulse lore, pulse measurement systems and different models of human cardiovascular system is given.
- **Chapter 3:** Brief review on physiology and functioning of human cardiovascular system is given.
- **Chapter 4:** The CVS model by M. Ursino is studied in detail. The model is simulated in Simulink and the results are discussed.
- **Chapter 5:** The CVS model by Leaning *et al.* is studied in detail.
- **Chapter 6:** A combined model of the above two models is developed. The model is simulated in Simulink and results are discussed.
- **Chapter 7:** Concludes the thesis and gives future direction of research.

The next chapter is on the literature survey that has been done on ancient pulse lores, pulse measurement systems and models of human cardiovascular system.

CHAPTER 2

LITERATURE SURVEY

2.1 Ancient Pulse Lores

The art of diagnosing diseases from blood pulse is known as pulse science or sphygmology. This science was extensively developed in Traditional Chinese Medicine and Indian Ayurvedic System[1]. Egyptian, Greek and Arabic civilizations also used pulse diagnosis, though they were not as extensive as it was in India and China. In all these civilizations, the medical practitioners used to diagnose the patients by just qualitatively measuring the blood pulse in the radial artery. Unlike the modern clinician who measure a single pulse, they measured three distinct pulses at the wrist.

2.1.1 Egyptian Pulse Lore

Pulse science was reported earliest in Egyptian civilization[1]. Here the pulse diagnosis centres around heart. To examine the pulse, the practitioner palpates the head, two hands and legs and heart. No procedural information about pulse examination or pulse signs with reference to diagnosis and prognosis was there.

2.1.2 Greek Pulse Lore

Galen, a popular medical practitioner from Greece wrote many treatises on pulse according to their length, breadth and depth[1]. The pulses were classified as Types of pulses like 'slow' & 'fast', 'regular' & 'irregular', 'strong' & 'feeble', 'wave-like', 'ant-like'. Method to determine normal and abnormal health from pulse was described. The diagnosis was qualitative in nature.

2.1.3 Chinese Pulse Lore

Pulse science was extensively developed in Chinese civilization[1]. The entire medical practice was based on theory of pulse. Three pulses are measured at the radial artery of both hands(2.1). They divided the extent of pulses into – 'taum' or 'inch', 'kwen' or 'bar', 'chi'ih' or' 'cubit'. Each of the above has internal or superficial and external or deep pulses. Various organs were related to different pulses. The principal pulses are superficial, deeep, slow and quick. The subsidiary pulses are Hua, Se, Hau, Shih, Ch'ang, Tuan, Hung, Wei, Chin, Huan, Koung, Hsein, Ke, Lao, Ju, Jo, San, His, Fu, Chich, Tai. Different combination of pulses indicates different diseases or health conditions. Also, pulse variations under season, age, constitution, temperament and sex were noted.

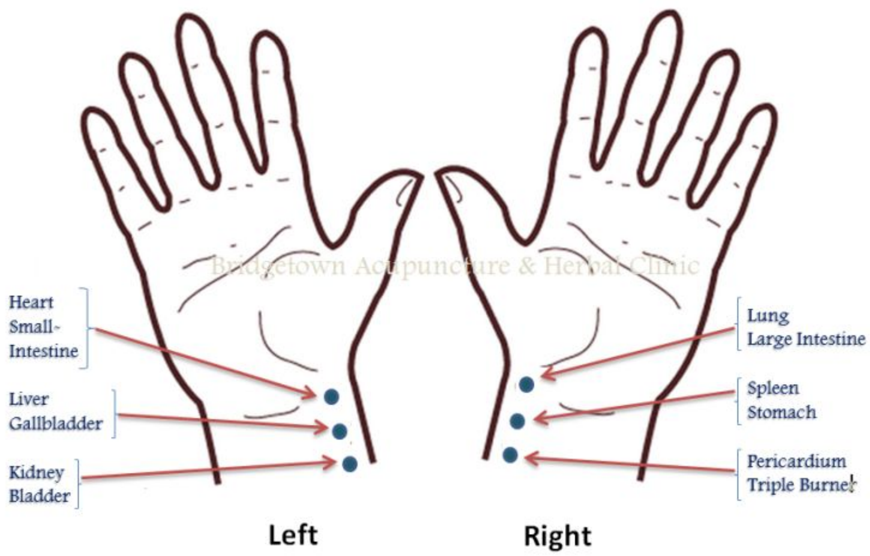

Figure 2.1: Chinse Pulse Diagnosis Chart[25]

2.1.4 Indian Pulse Lore

In Indian civilization pulse science was an outcome of Yoga which deals with other things with pulse and breath control[1].Pulse movements in terms of animals like horses, reptiles, amphibians, birds etc. were mentioned. The Tamil Siddhars classified pulses according to nature, action and other characteristics – Tivranadi(fast pulse), Thallunadi(irregular), Nerungiyanadi(tense), Gatinadi(flowing and hard), Abalanadi(weak), Idaividunadi(interrupted), Thadangunadi(slow), Ozungunadi(normal). Three pulses are measured at the radial artery and are termed Vata, Pitta and kapha(2.2). They correspond to the Vata, Pitta and Kapha zones of the body.

FIGURE 2.2: Vata Pitta Kapha[1]

In India, the Tridosha theory[10] was prevalent and the three pulses in the radial artery contained information about the derangement of Doshas. The human body can be conceptualised as three zones named Kapha, Pitta and Vata(2.3). The Kapha zone includes the section of body from head to lungs where effect of cold is dominant. Pitta zone constitutes the part of body from below lungs to the small intestine and abdomen where the digestion occurs. The part from lower abdomen till legs is known as Vata where the effect of gaseous elements due to indigestion are dominated.

2.2 Pulse Measurement System

Some works are existing on the development of three pulse measurement system. Nadi Yantra[12] measures the three pressure pulses using piezo sensors and suitable signal conditioning. In Nadi Aridhal[13] an attempt is done to diagnose disease

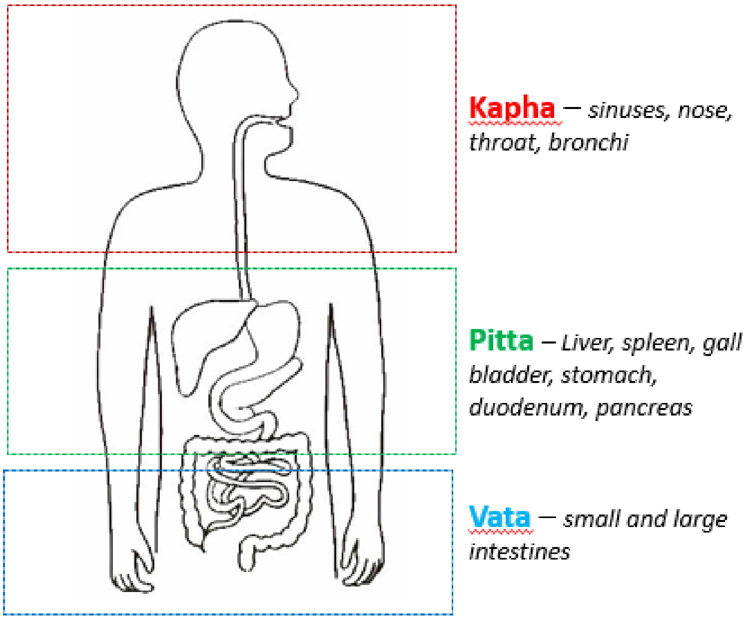

Figure 2.3: Associated Regions of Human Body in Tridosha Theory[10]

by analysing the measured three pulses. In Nadi Tarangini[14] diaphragm with strain gauge on it as the primary sensor for pressure measurement.

2.3 Models of Human Cardiovascular System

Many models on human cardiovascular system are available in the literature. The models vary in complexity and purpose. Some focus on arterial haemodynamics while others focus on baroreflex and nerve control. In [9] a complete lumped-parameter model with short-term homeostatic control is developed with focus on simulation of haemodynamic response to gravitational stress.

The arterial tree has been represented as linear lumped Windkessel model in many works[2, 3]. In [15] along with lumped model, characteristic impedance is also introduced. The advantage is that transmission phenomena can be analysed. Electrical transmission line model is done in [16]. The pressure wavefroms were more accurate in aorta, but there was significant error in peripheral artery. An electronic equivalent of the system is developed in [17]. In this work, the whole systemic circulation is represented using a few components. One dimensional nonlinear model of blood flow in arteries is given in [18]. Though accurate, it is suitable to reprensent a section of blood vessel. Trying to model whole haemodynamics of the

CVS using this approach may be overwhelmingly complex. In [7] the system is represented as an electric model where the pumping of heart is represented using pulse generator.In many works including [2, 3, 8, 9] the pumping heart has been represented using time varying elastance function.

On simulation of cardiovascular system probably the first work is [19]. It has undergone simulation in many platforms, of which the latest is Simulink. The modelling is based on assumptions such as, blood is without mass, blood is Newtonian, lumped parameter system, linear compliance and valves close instantaneously. Recent works in the area are [20–23]. A detailed work is in [24].

For modelling any system, a detailed understanding of the system is required. Here, since we are interested in modelling the human cardiovascular system, understanding the physiology and functioning of the same is necessary. Hence the next chapter is on physiology of the CVS and its various functions.

CHAPTER 3

PHYSIOLOGY AND FUNCTIONING OF HUMAN CARDIOVASCULAR SYSTEM

3.1 Introduction

There are many organ systems in the human body which has been conceptualised based on their functionality. The cardiovascular system is one among them which carries out the roles of transporting oxygen, nutrients and other chemicals throughout the body. It is a closed loop system which consists of the heart, vascular system and blood. A secondary function of the system is thermoregulation of the body.

The blood is the fluid which acts as the transmission medium for oxygen, nutrients and chemicals. The blood is circulated throughtout the body due to the pumping action of heart.

[? ?] has been referred to learn about the physiology and functioning of CVS.

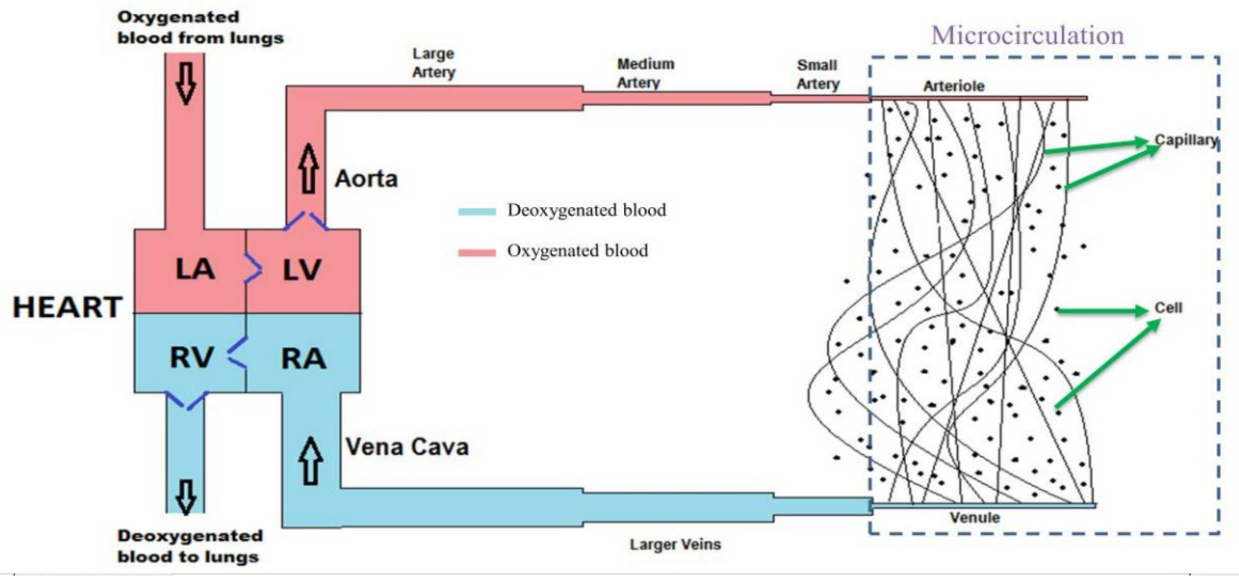

Figure 3.1: Conceptual Model of Cardiovascular System

As shown in the figure(3.1) while the blood is being circulated in the body, it gets oxygenated in the lungs and gets de-oxygenated for respiration in the cells. The pressure gradient required for circulation of blood is generated by the pumping action of blood.

3.2 Physiology of Cardiovascular System

The components of the CVS are the heart, blood and vascular system.

3.2.1 Heart

Heart is the pump-house of CVS. It composes of four chambers, viz., right atrium(RA), left atrium(LA), right ventricle(RV) and left ventricle(LV)(3.2). There is a uni-directional valve between RA and RV known as tricupsid valve and the one between LA and LV is bicupsid valve. The pulmonary valve separates right ventricle and pulmonary artery whereas the aortic valve separates aorta and left ventricle. The tricupsid and bicupsid valves are collectively known as atrioventricular valves and the pulmonary and aortic valves are known as semilunar valves. The deoxgygenated blood from different parts of the body enters the RA, passes to RV through tricupsid valve. From LV, the blood is pumped to lungs and is oxygenated there. The oxygentaed blood enters LA and passes to LV through bicupsid valve. From LV the oxygenated blood is pumped to all parts of the body.

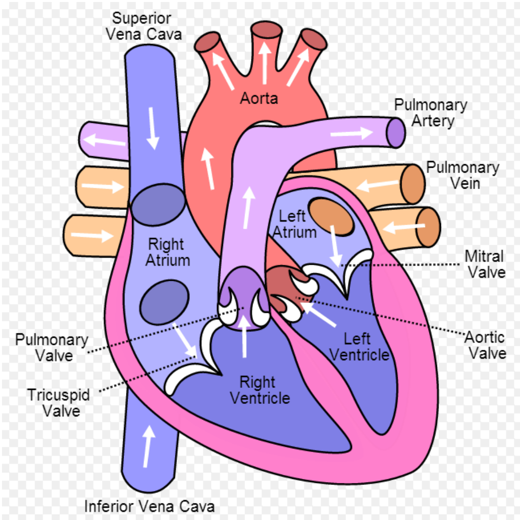

FIGURE 3.2: The Human Heart (courtsey: Wikipedia)

The pumping of heart generates sufficient pressure to circulate blood throughout the body. The contraction of atria happens first, and then the ventricles contract. The contraction is triggered by depolarization of the plasma membrane which initially occurs at the Sino Atrial(SA) node. The depolarization then spreads through the muscle cells of atria. Subsequently it spreads and reaches the AtrioVentricular(AV) node which causes contraction of ventricles.

3.2.2 Blood

Blood carries oxygen and nutrients to approximately 10^{14} cells in the body. It is a heterogeneous solution of blood cells in plasma. The blood cells comprises of Red Blood Cells(RBC), White Blood Cells(WBC) and platelets. Each component has a specific functioning the body. The RBC aids transport of blood gases, WBC identifies and disposes foreign substances, and platelets aid in clotting. Plasma is a fluid which is almost twice as viscous as water. They contain the nutrients such as glucose, electrolytes, vitamins, minerals, enzymes etc. that has to be supplied to cells. In a normal human body there is around five litres of blood which constitutes about 8% of body weight.

3.2.3 Vascular System

The whole vascular system is a closed loop network which consists of the arteries, arterioles, capillaries, venules and veins(3.3). All the vessels act like a conducting pipe and has a common inner lining.

The different circulation in the body are pulmonary(lungs), skeletal(bones), coronary(heart), cerebral(brain), renal(kidney), cutaneous(skin), hepatic(liver) and splanchnic(stomach and intestines) circulations.

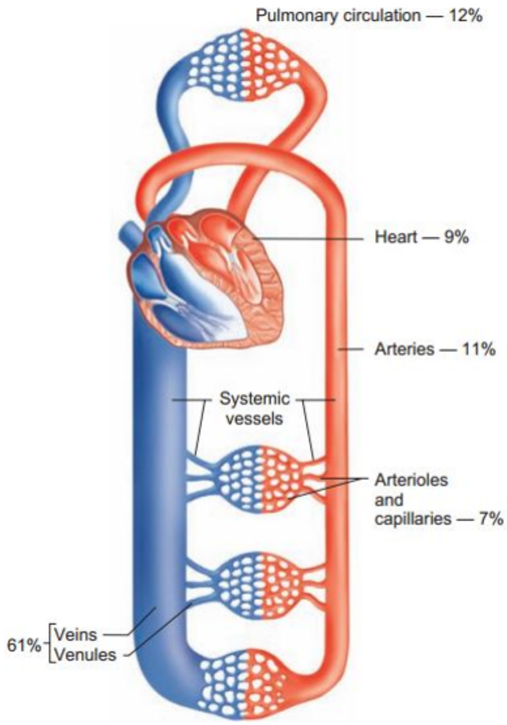

FIGURE 3.3: The Vascular System[4]

3.2.3.1 Artery

Arteries carry blood away from the heart. The largest artery is the aorta. According to size the arteries are divided into central(aorta), intermediate (carotid and brachia) and peripheral (radial and femoral). The larger arteries are more elastic in nature whereas the smaller ones are less compliant. The elasticity of the walls allow the arteries to act as a pressure reservoir and makes sustained flow of blood possible. During systole, when blood is pumped into the artery, it extends and stores the blood. Later during diastole, the wall recoils and flow of blood is continued. The mean pressure in the arteries is around 95-100 mmHg.

Pulmonary arteries carry de-oxygenated blood from right ventricle to lungs whereas systemic arteries carry oxygenated blood from left ventricle to other parts of the body.

3.2.3.2 Arterioles

The smaller arteries again branch into arterioles which supply blood to organs. The resistance of arterioles are significantly higher than arteries. The walls of arterioles are not elastic. The diameter of artrioles are controlled to adjust the amount of blood flow to the respective organs. Therefore the arerioles play a major role in detrmining the mean arterial pressure.

3.2.3.3 Capillaries

Capillaries perform the ultimate function of cardiovascular system which is exchange of nutrients and gases between cells and blood. The proximity of capillary to a cell is around 0.1 mm. The exchange happens, therefore, via diffusion(3.4).

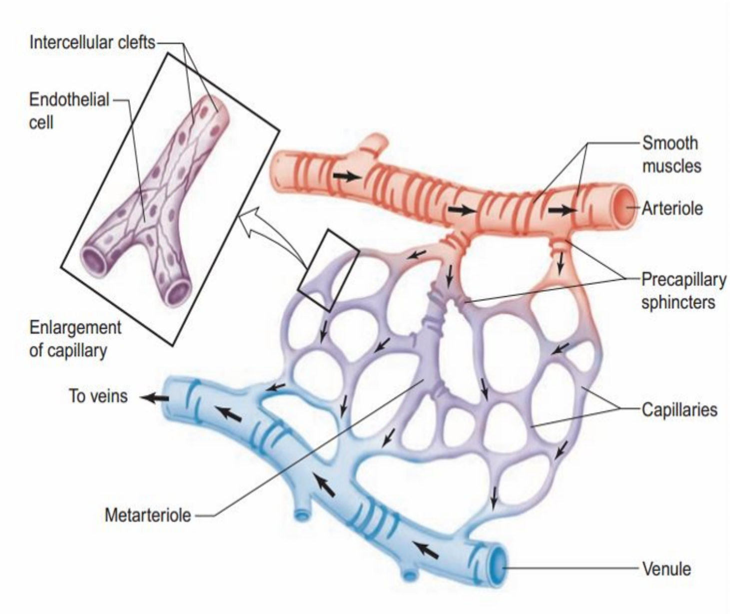

FIGURE 3.4: Capillaries[4]

3.2.3.4 Veins

Veins carry de-oxygenated blood from different parts of the body towards the heart. They have larger diameter and is more compliant. The largest vein is known as vena cava which is divided into superior and inferior vena cava. The mean pressure in veins is around 10-15 mmHg.

3.3 Functioning of Cardiovascular System

3.3.1 Cardiac Cycle

In a normal human, the heart pumps 72 times per minute. The sequence of events between two consecutive beats is known as cardiac cycle. The events are divided into four(3.5):

1. **Isovolumetric Ventricular Contraction** - Both the atrioventricular valves and semilunar valves are closed. The electrical impulses reach the ventricular muscle cells and causes the ventricles (both right and left) to contract. Since the contraction happens with constant volume, it is known as isovolumetric contraction. During this period the pressure in the left ventricle rises sharply.

2. **Ventricular Ejection** - The pressure rise inside the ventricles causes the semilunar valves to open and blood from ventricles are ejected into the respective arteries.

3. **Isovolumetric Ventricular Relaxation** - Both atrio-ventricular and semilunar valves are closed and the ventricles relax, dropping the pressure inside them. Since the volume is constant it is termed isovolumetric relaxation.

4. **Ventricular Filling** - The atria contract and it causes atrio-ventricular valves to open and subsequently blood fills the ventricles.

Events 1 and 2 is collectively known as the systole and 3 and 4 is known as diastole. Normally, systole is 300 ms and diastole is 530 ms.

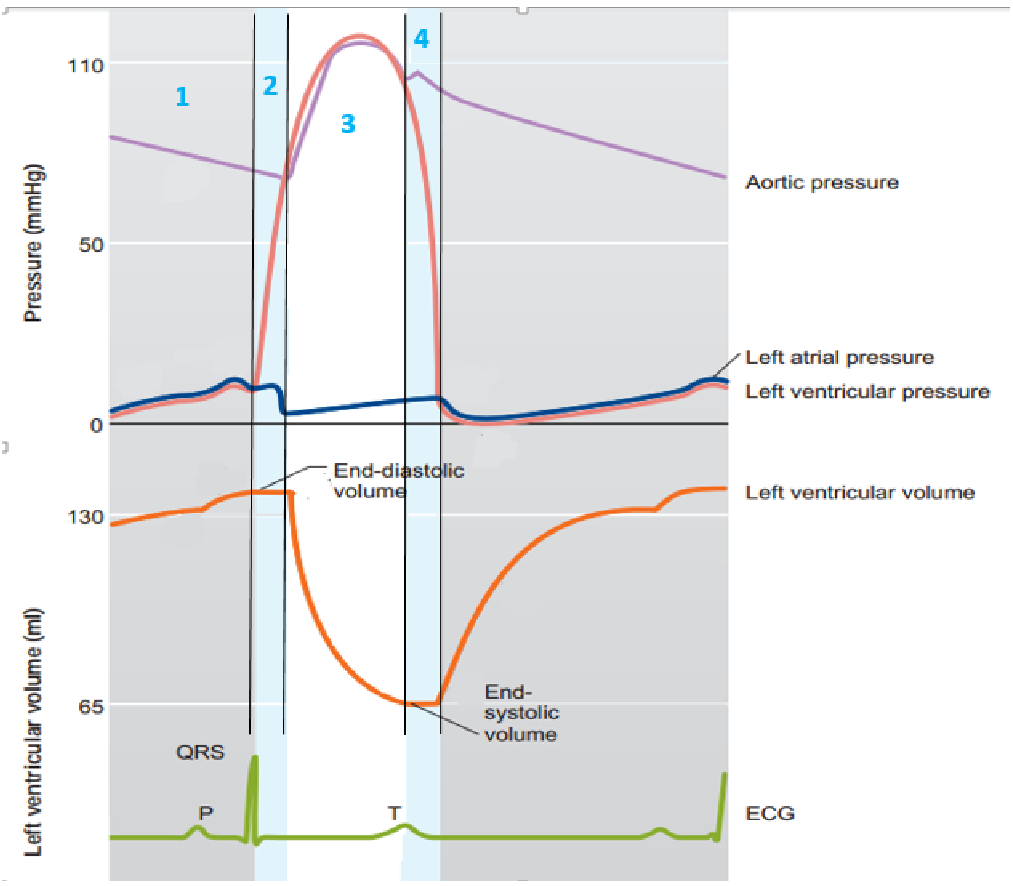

FIGURE 3.5: Pressure and Volume during Cardiac Cycle[4]

The volume of blood in left ventricle after diastole and systole are known as End Diastolic Volume (EDV) and End Systolic Volume (ESV) respectively3.5. The amount of blood expelled to different parts of the body during a cardiac cycle is known as Stroke Volume (SV). The volume of blood pumped by heart in a minute is known as Cardiac Output(CO).

$$SV = EDV - ESV \tag{3.1}$$

$$CO = HR * SV \tag{3.2}$$

3.3.2 Haemodynamics and Pulse Formation

The factors such as blood pressure, blood flow and resistance to blood flow are collectively known as haemodynamics. Blood flow is caused by difference in pressure, which is in turn caused by the contraction of heart. Volumetric flow rate is given by:

$$F = \frac{\Delta P}{R} \tag{3.3}$$

where R is the resistance to blood flow and depends on the diameter of the vessel(d), blood viscocity (η), and length of vessel(L):

$$R = \frac{8 * L * \eta}{\pi * r^4} \tag{3.4}$$

3.3.2.1 Pulse Formation

The blood pulse[1] is a pressure wave of distension caused by the systolic ejection of blood into the arteries by heart. The elasticity of arteries play a major role in pulse formation. Sudden ejection of blood into the artery distends them and causes bulging. Subsequently, the pressure arises and the blood moves to the next point and the pressure wave reaches the next point. This is repeated as the pulse progresses away from heart. Pulse velocity solely depends on the elastic property of the artery and hence it has higher velocity in peripheral arteries.

The pulse waveform in the aorta has a sharp initial rise, and a short sharp trough called incisura. As the pulse propagate further away from heart it is shifted and altered. The insicura is damped(3.6). They are due to effects of damping and reflected waves.

3.4 Cardiovascular Control

There is an inherent control system in the cardiovascular system which prioritizes different parts of body that has to be selectively perfused according to metabolism and function. The organs are prioritized based on how essential they are to maintain life (brain, heart), to respond to life threatening situation (muscle so limbs to

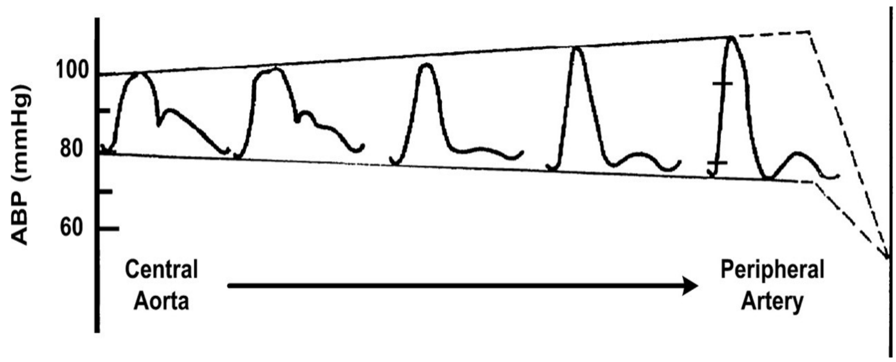

FIGURE 3.6: Blood Pulse Propagation [11]

run in a fight or flight situation) and how well they survive with decreased supply of blood (smooth muscles with anaerobic capability).

There are two types of control(3.7): intrinsic and extrinsic. The intrinsic control is based on inherent physiochemical attributes of organs. For example, capillary widens when waste accumulates and causes more blood to flow in. The extrinsic control is caused by sympathetic and parasympathetic nerves. For example, in extreme cold the sympathetic nerve causes arterioles to constrict to reduce blood flow to prevent heat losses.

The controlling is done by varying heart rate, EDV, ESV, arteriolar resistance, blood volume and/or blood composition.

3.5 Arterial Pressure Regulation

There is an internal mechanism to regulate the mean pressure in the arteries. It is known as baroreflex control system. Pressure sensors known as baroreceptors are located in the carotid artery and aortic arch. When there is variation from the normal mean pressure, the sympathetic and parasympathetic nerves act so as to counteract the change in pressure and regulate the pressure at normal value. The baroreflex mechanism is a short term regulation mechanism.

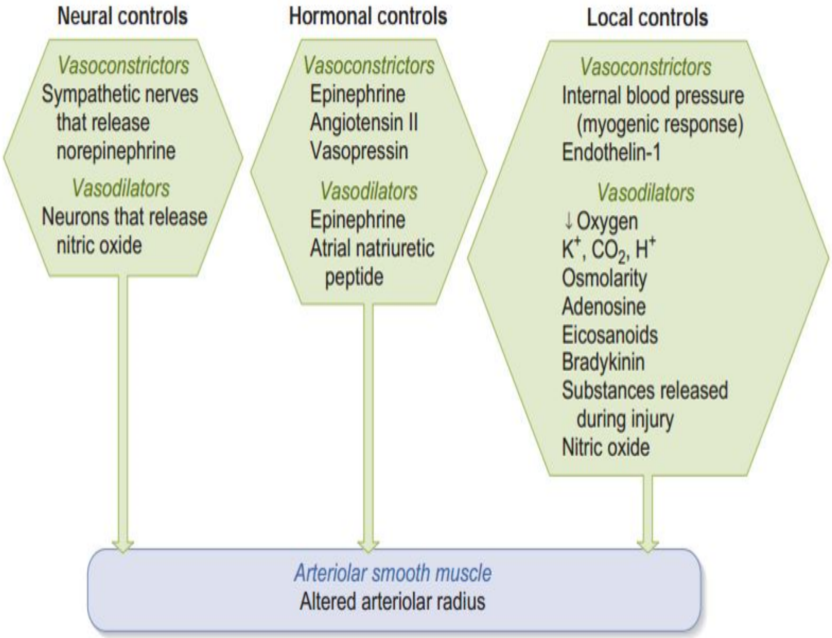

FIGURE 3.7: Cardiovascular Control[4]

Once we have an understanding about a system, the next step is to construct a mathematical model of the system. Existing models of the CVS are explained in the next two chapters. A model by M. Ursino[2] is explained in the next chapter.

CHAPTER 4

CARDIOVASCULAR MODEL BY M. URSINO

4.1 Introduction

This chapter explains a model of the cardiovascular system developed by M. Ursino[2]. In this model the CVS is essentially treated as a hydrodynamic system comprising of a pump, water and pipes which are analogous to the heart, blood and blood vessels respectively.

Mathematically the pumping of the heart is modelled as a varying elastance function. The vascular system is modelled using linear lumped differential equations originating out of the elasticity of the vessel walls, resistance of walls to flow and inertia of the fluid volume.

4.2 Hydrodynamic Model

The whole cardiovascular system is divided into the heart and vascular systems. The vascular system is divided into eight segments:

- Pulmonary circulation - pulmonary arteries (pa), pulmonary peripheral circulation (sv), pulmonary veins (pv)
- Systemic arteries (sa)
- Splanchnic circulation - splanchnic peripheral circulation (sp), splanchnic veins (sv)
- Extrasplanchnic circulation - extrasplanchnic peripheral circulation (ep), extrasplanchnic veins (ev)

The heart has four chambers:

- Right Atrium (ra)
- Right Ventricle (rv)
- Left Atrium (la)
- Left Ventricle (lv)

Each segment is modelled using three lumped parameters which are flow resistance(R), compliance of vessel wall(C) and intertance of fluid volume(L).

4.2.1 Flow Resistance

When fluid flows through a pipe(4.1) there will be two sources of resistances : one is due to the friction between the pipe wall and fluid and other is the friction between different layers of the fluid. This resistance causes the pressure to drop along the wall. This is analogous to resistance in an electrical circuit which causes the voltage to drop.

The resistance depends on the area of the pipe, viscosity of the fluid and the length of the pipe. The mathematical expression is given as follows. The standard unit is Pa.s/m^3.

$$R = \frac{8 * L * v}{\pi * r^4} \tag{4.1}$$

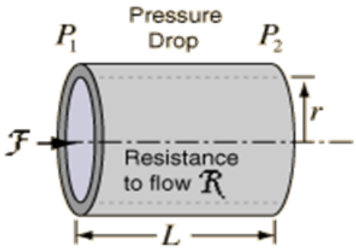

Figure 4.1: Flow through a pipe

L - length of pipe (m)
v - viscosity of fluid (Pa.s)
r - radius of the pipe(m)

Poiseulle's law gives a relation between volumetric flow rate and pressure drop in a pipe(eqn: 4.1). The assumptions are that the fluid is incompressible and Newtonian and the flow is laminar.

$$Q = \frac{P_1 - P_2}{R} \tag{4.2}$$

Q - Volumetric flow rate (m^3/s)
P_1 and P_2 - pressure at both ends (Pa)

4.2.2 Compliance

The elasticity of a vessel wall is represented using the parameter known as compliance. For an elastic pipe, it is defined as the ratio between the change in volume in the pipe to the change in pressure across the pipe.

$$C = \frac{\Delta V}{\Delta P} \tag{4.3}$$

ΔV - Change in volume (m^3)
ΔP - Change in pressure (Pa)

To understand the concept of compliance intuitively, consider a balloon filled with water. A balloon with higher compliance can increase the volume by filling in more water without increasing the pressure significantly. This is evident from the equation given above(eqn: 4.3).

The parameter analogous to compliance in electric circuits is capacitance which is the ratio of charge and voltage. Higher the capacitance, higher the charge that can be stored in the capacitor at the same voltage.

The inverse of compliance is known as the elastance (eqn: 4.4).

$$E = \frac{1}{C} \tag{4.4}$$

4.2.3 Inertance

The inertial effects of volume of blood is represented using intertance. It is defined as the pressure difference in a fluid required to cause a change in volumetric flow rate. Inertance of a tube is given by the following equation(eqn: 4.5).

$$L = \frac{\rho * l}{A} \tag{4.5}$$

ρ - density of fluid (m^3/kg)
l - length of tube(m)
A - area of the tube(m^2)

In electric circuits and analogous parameter is inductance.

4.2.4 Overall Model Representation

This is a simplified model of the highly complex cardiovascular system(4.2). The approximations made are:

- Blood is assumed to be incompressible and Newtonian.
- The vessels are modelled using linear lumped parameters.
- The complex morphology, non-linear walls and multiple levels of homoeostatic systems are neglected.
- Elasticity of the blood vessels are assumed to be constant.

In the original work by M. Ursino the baroreflex control and action of parasympathetic and sympathetic nerves are also taken into account. But here we neglect that for simplicity.

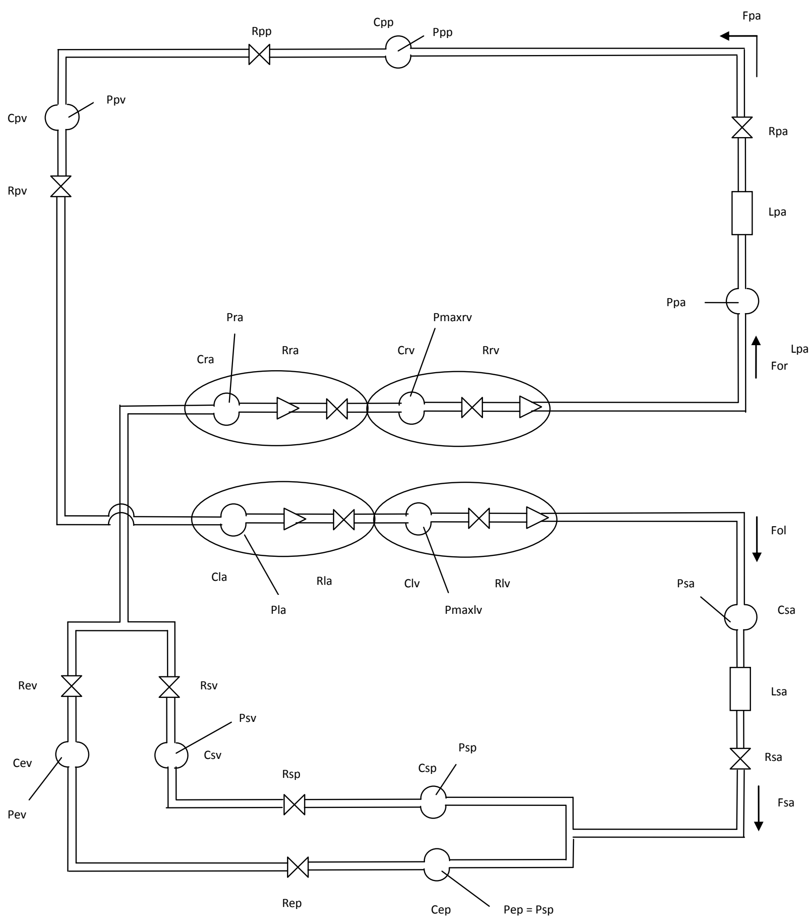

FIGURE 4.2: Hydrodynamic Model of Cardiovascular System

4.3 Mathematical Model

4.3.1 Heart

Consider left heart(4.3)

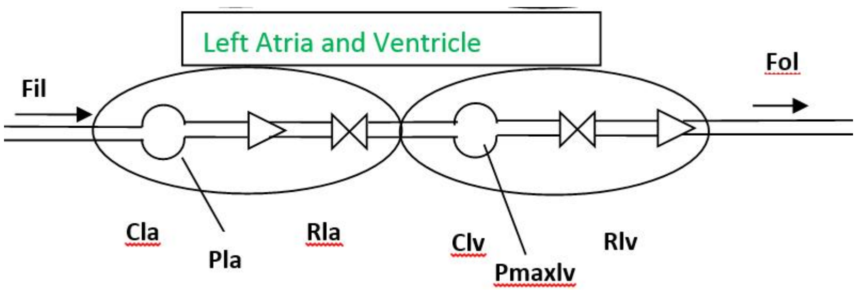

FIGURE 4.3: Hydrodynamic Model of Heart

- C_{la}, L_{la} and R_{la} are the compliance, inertance and resistance of the left atrium.
- C_{lv} and R_{lv} are compliance and resistance of left ventricle.
- P_{maxlv} is the maximum left ventricular pressure.

Atria and ventricles are modelled as varying elastance. That is, its compliance is a non-linear function of time.

No fluid volume is stored in C_{la}. Therefore the rate of change of volume should be proportional to the difference in flow rate. Applying conservation of mass across C_{la} we get

$$\frac{dV_{la}}{dt} = \frac{1}{C_{la}}(\frac{P_{pv} - P_{la}}{R_{la}} - F_{il}) \tag{4.6}$$

Flow only when mitral valve is opened.This is modelled using a switch.

$$F_{il} = \begin{cases} 0 & : if P_{la} \leq P_{lv} \\ \dfrac{P_{la} - P_{lv}}{R_{la}} & : P_{la} \geq P_{lv} \end{cases} \tag{4.7}$$

Applying conservation of mass in left ventricle

$$\frac{dP_{lv}}{dt} = F_{il} - F_{ol} \tag{4.8}$$

Flow from left ventricle to aorta when aortic valve opens

$$F_{ol} = \begin{cases} 0 & : if P_{maxlv} \leq P_{sa} \\ \dfrac{P_{maxlv} - P_{sa}}{R_{lv}} & : P_{maxlv} \geq P_{sa} \end{cases} \tag{4.9}$$

P_{maxlv} is the isovolumetric left ventricular pressure

Resistance of valve varies with P_{maxlv}

$$R_{lv} = k_{Rlv}.P_{maxlv} \tag{4.10}$$

P_{maxlv} is exponential at diastole and linear in during systole

$$P_{maxlv} = \varphi(t).E_{maxlv}.(V_{lv} - V_{ulv}) + [1 - \varphi(t)].P_{0lv}.e^{((k_{Elv}.V_{lv})-1)} \tag{4.11}$$

- E_{maxlv} is ventricle elastance at maximum contraction
- V_{ulv} is the unstressed volume of left ventricle
- P_{0lv} and K_{elv} are constants
- $\varphi(t)$ is the activation function

The activation function is given by

$$\varphi(t) = \begin{cases} sin^2[\dfrac{\pi.T(t)}{T_{sys}(t)}.u] & : 0 \leq u \leq \dfrac{T}{T_{sys}} \\ 0 & : \dfrac{T}{T_{sys}} \leq u \leq 1 \end{cases} \tag{4.12}$$

- where E_{maxlv} is T is the heart period
- T_{sys} is the period of systole

u is a function known as 'integrate and fire'. It resets to zero as soon as it reaches 1.

$$u(t) = frac[\int_{t_0}^{t} \frac{1}{T(\tau)} d\tau + u(\tau_0)] \tag{4.13}$$

Similar set of equations are applied to right atrium and ventricle.

4.3.2 Vascular System

The blood vessels are modelled using linear lumped parameters: the resistance, compliance and inertance. This results in first order differential equations(4.4).

Consider pulmonary circulation

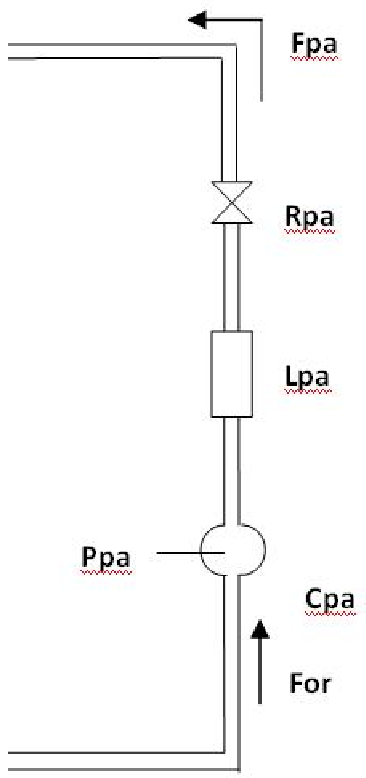

FIGURE 4.4: Hydrodynamic Model of Pulmonary Circulation

Applying conservation of mass across C_{pa}

$$\frac{dP_{pa}}{dt} = \frac{F_{or} - F_{ir}}{C_{pa}} \tag{4.14}$$

Across L_{pa} the rate of change of flow rate is proportional to pressure drop across the segment. Applying balance of forces (since pressure is force per area) we get

$$\frac{dF_{pa}}{dt} = \frac{P_{pa} - P_{pp} - R_{pa}F_{pa}}{L_{pa}} \tag{4.15}$$

Applying the same concept, the equations for other vascular segments are found.

4.4 Simulation

The model has been simulated by [6] in Simulink(4.5). The model is simulated with minor modifications and the pressure waveforms at left ventricle, left atrium, and aorta and volume at left ventricle has been generated(4.6).

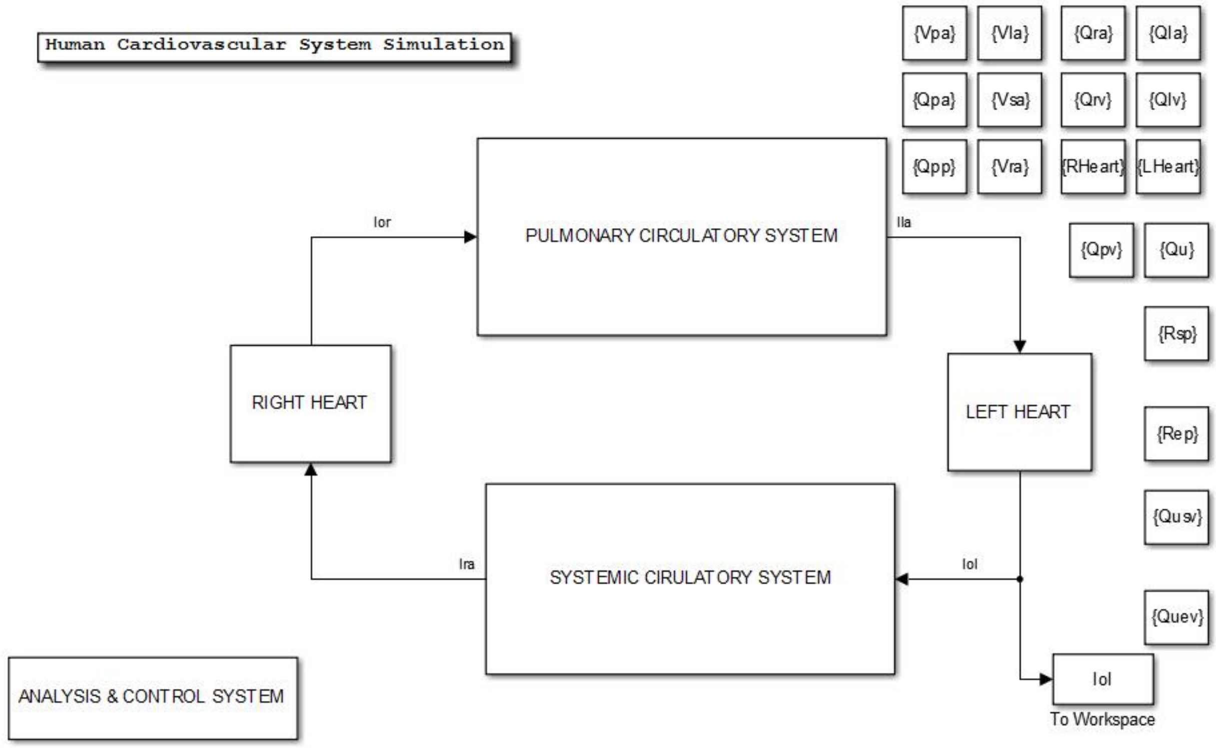

FIGURE 4.5: Simulink block diagram of M.Ursino model[6]

We see that the simulated result is very similar to the actual waveforms(fig. 3.5)

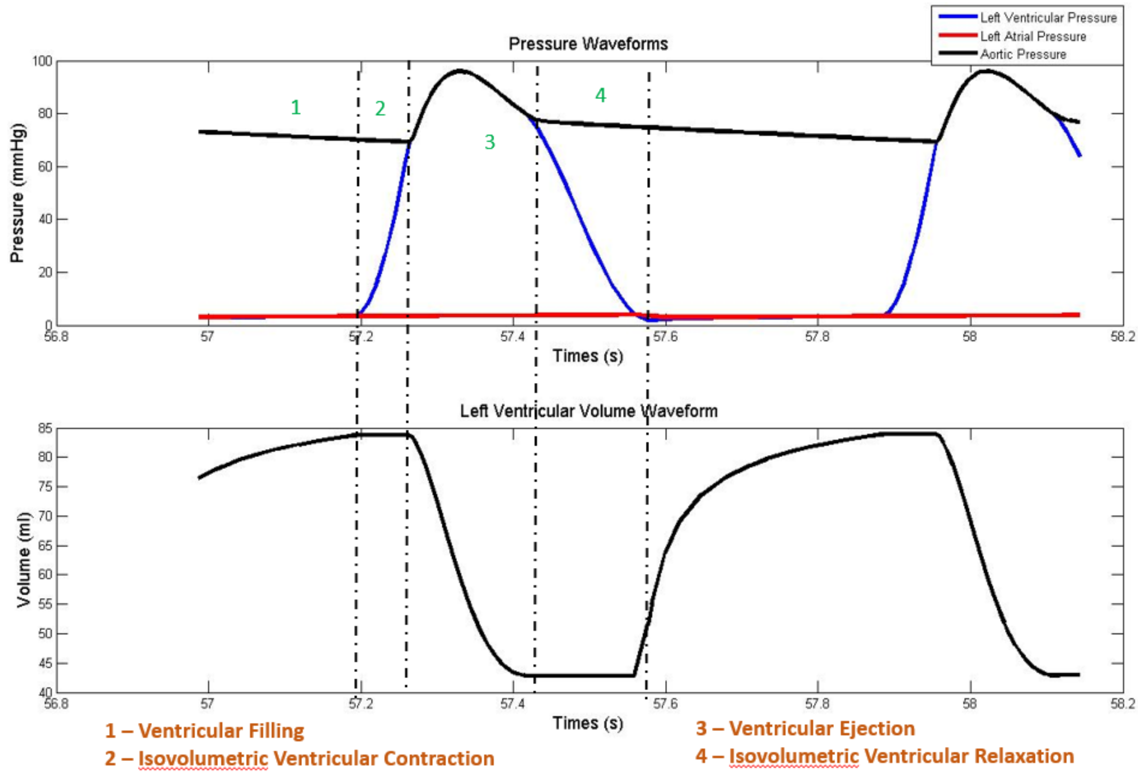

Figure 4.6: Pressure Waveforms generated in M.Ursino model

Leaning *et al.*[3] has developed a model of the CVS. The model gives an elaborate representation of the vascular system and also considers the gravitational effects on the orientation of the vessels. Studying of this model will be highly useful to obtain a model which gives pressure waveforms at the radial artery. Next chapter explains this model.

CHAPTER 5

CARDIOVASCULAR MODEL BY LEANING *ET AL.*

5.1 Overall Model

In the model[3] the heart is represented as an varying elastance model. Pulmonary circulation is divided into pulmonary arteries and pulmonary veins. The systemic circulation is comprised of seven arterial segments and six vein segments(5.1).

The vascular system is modelled with lumped parameters which are hydrodynamic resistance that opposes flow, the compliance which indicates how much volume changes with a given pressure differential, and the inertance which determines the pressure difference required to change the flow rate.

Compared to the model by M. Ursino, this model has represented the vascular system in more detail. Hence studying this model will be highly useful to obtain a model which gives pressure waveforms at the radial artery. The present model has taken into account the effect of gravity on the blood pressure in arteries depending on their orientation.

In the work by Leaning *et al.* representation of baroreflex control, neural control and effect of drugs is also included. Here they are neglected for simplicity.

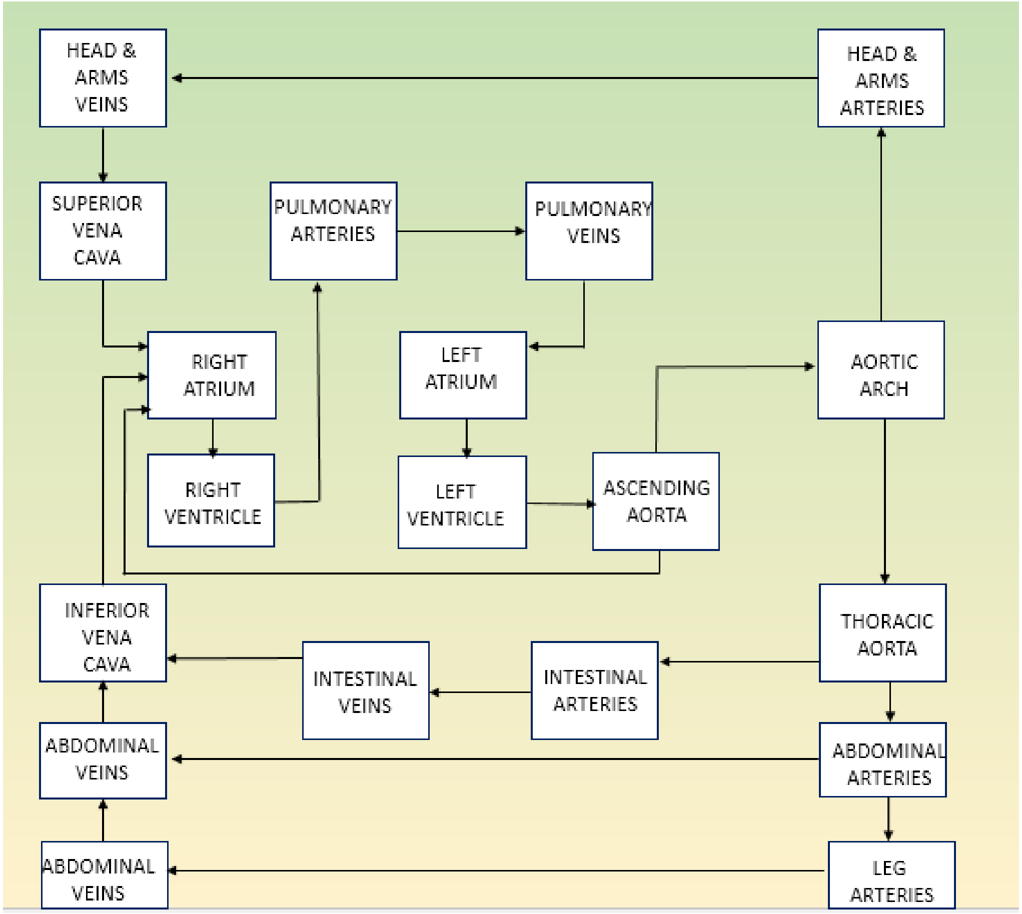

FIGURE 5.1: Model of Cardiovascular System by Leaning *et al.*[3]

5.2 Mathematical Model

The blood vessels are modelled using lumped parameters: the resistance, compliance and inertance. This results in first order differential equations.

The equations are found by applying two important concepts, conservation of mass and balance of forces. Across a compliance, the volume change rate is equal to the algebraic sum of flow rates into and out of it. Similarly in an inertance the change in flow rate is caused due to the pressure difference and losses across it.

There are 19 segments in the model. For all segments j with i as previous segment and k as next segment considering direction of flow :

$$\frac{dV_j}{dt} = \Sigma_i F_{ij} - \Sigma_j F_{jk} \tag{5.1}$$

5.2.1 Arterial Segments

For an arterial segment the resistance, compliance and geometry are taken into account. We get linear differential equations for the model of the segments as follows. Consider j^{th} arterial segment

$$\frac{dF_{jk}}{dt} = (\frac{P_j - P_k - R_{jk}F_{jk} - G_{jk}}{L_k}), \forall k \tag{5.2}$$

where G_{jk} is the pressure gradient between j^{th} and k^{th} segments due to gravity

$$G_{jk} = gl_{jk}sin\phi_{jk} \tag{5.3}$$

Prssure in the j^{th} segment is given by

$$P_j = \frac{V_j - V_{uj}}{C_j} + \frac{K_j}{C_j}\frac{dV_j}{dt} \tag{5.4}$$

5.2.2 Heart Segments

There are four heart segments or chambers which are right and left atria and right and left ventricles. Their pumping is represented as unidirectional pumps. The pumping action is expressed by the following relation between pressure and volume

$$P_j = a_j(t)(V_j - V_{uj}) \tag{5.5}$$

where a(t) is the time varying elastance function.

For ventricle segments : Using balance of forces, the equation for ouflow from ventricle is given as

$$\frac{dF_{jk}}{dt} = \frac{P_j - P_k - R_{jk}F_{jk} + F_{jk}^2(\frac{\rho}{2A_j^2})}{L_j}, F_{jk} \geq 0 \tag{5.6}$$

The respective elastance function is given by

$$a_j(t) = y(b_2 a_{jS} - a_{jD}) + a_{jD} \tag{5.7}$$

where

$$y = \begin{cases} 0 & : t_c < T_{AV} \quad or \quad t_c > T_{AV} + T_{VS} \\ sin(\dfrac{\pi(t_c - T_{AV})}{T_{VS}}) & : T_{AV} \leq t_c \leq T_{AV} + T_{VS} \end{cases} \tag{5.8}$$

Similarly for atrial segments: The flow equation is

$$F_{jk} = \frac{P_j - P_k}{R_{jk}}, F_{jk} \geq 0 \tag{5.9}$$

with respective elastance function

$$a_j(t) = x(b_2 a_{jS} - a_{jD}) + a_{jD} \tag{5.10}$$

where

$$x = \begin{cases} 0 & : t_c > T_{AS} \\ sin(\dfrac{\pi t_c}{T_{AS}}) & : tc \leq T_{AS} \end{cases} \tag{5.11}$$

For a heart period of 0.8s, $T_{AS} = 0.172$s, $T_{AV} = 0.132$s and $T_{VS} = 0.32$s.

5.2.3 Venous Segments

Veins have high compliance and they act as large-capacity vessels with low transmural pressure. Therefore model is nonlinear. For any venous segment j: Relation between pressure and volume is

$$P_j = \frac{V_j - V_{uj}}{C_j} \tag{5.12}$$

where the compliance becomes twenty times the value when the volume become less than the unstressed volume

$$C_j = \begin{cases} C_j & : V_j > V_{uj} \\ 20 * C_j & : V_j \leq V_{uj} \end{cases} \tag{5.13}$$

The equation for flow is nonlinear

$$F_{jk} = \left\{ \begin{array}{cc} \dfrac{(P_j - P_k)V_j^2}{R_{jk}V_{uj}^2} & : P_j \geq P_k \\ \dfrac{\beta_j(P_j - P_k)V_j^2}{R_{jk}V_{uj}^2} & : V_j \leq V_{uj} \end{array} \right\} \forall k \tag{5.14}$$

where k is the next segment.

The variables involved in the above equations are :

V - Volume (m^3)
V_u - Unstressed Volume
F - Volumetric Flow (m^3/s)
P - Pressure (mmHg)
R - Flow Resistance (mmHg.s/m^3)
C - Compliance (m^3/mmHg)
g - Acceleration due to gravity (m/s^2)
l - length of the segment (m)
ϕ - Orientation angle of segment (degree)
β_j - Constant

The left ventricular and aortic pressure waveforms generated using the model by M. Ursino was similar to the waveforms measured in vivo(fig: 3.5). The model by Leaning *et al.* gives an elaborate representation of the vascular system and also considers the gravitational effects on the orientation of the vessels. To exploit the advantages of both models, they are combined into a single model in which the heart representation is taken from the former and the representation of the vascular system is taken from the latter.

CHAPTER 6

COMBINED MODEL

To exploit the advantages of models by both M.Ursino[2] and Leaning *et al.*[3], they are combined into a single model in which the heart representation is taken from the former and the representation of the vascular system is taken from the latter.

6.1 Comparison between Two Models

A comparision between the two models gives:

Segment	**Model by M. Ursino**[2]	**Model by Leaning *et al.***[3]
Atrium and Ventricle	Varying Elastance – linear or exponential variation depending on systole or diastole, viscous losses are considered	Varying Elastance – sinusoidal variation
Artery	Compliance, Inertance and Flow Resistance	Compliance, Inertance and Flow Resistance, gravity effect on segments is considered
Vein	Compliance and flow resistance	Compliance and Flow Resistance , compliance varies depending on pressure difference between two segments
Systemic Circulation	3 segments	13 segments

Table 6.1: Comparison between Two Models

The model by M.Ursino represented the pulsating heart using a varying elastance model with which gives reasonably accurate pressure waveforms in the left ventricle and aorta. The model by Leaning *et al.* gives an extensive model of the vascular system. We try to develop a model in which the representation of heart is taken from M.Ursino's model and the representation of arteries and veins from Leaning *et. al*'s model.

6.2 Combined Model

The combined model looks like the following(6.1):

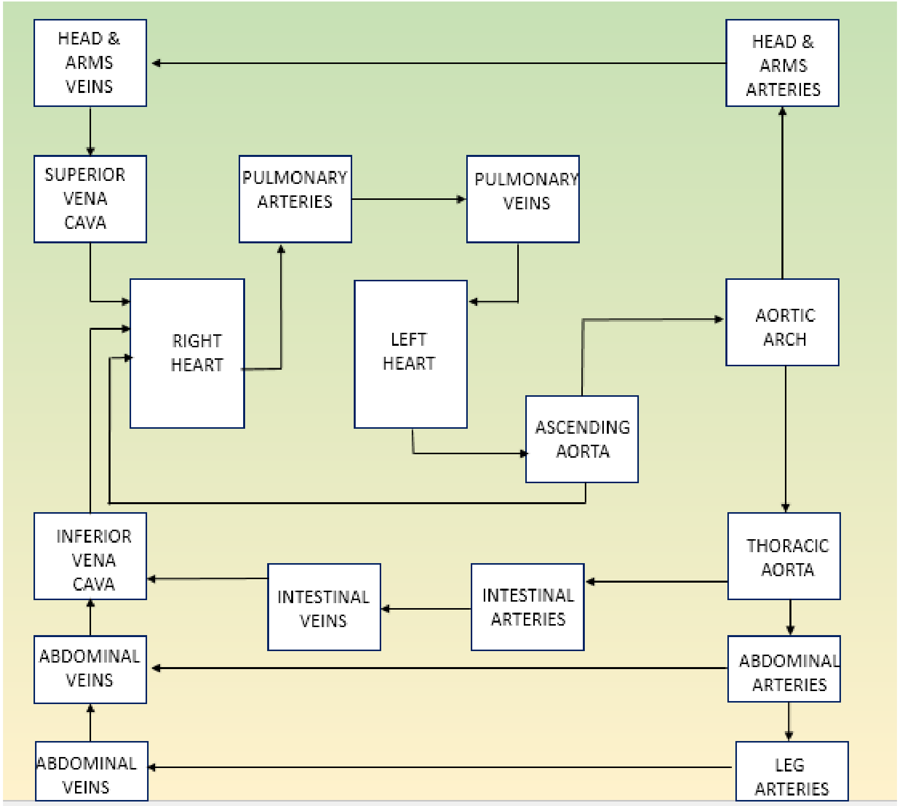

FIGURE 6.1: Combined Model

6.3 Simulation in Simulink

The electrical model of the cardiovascular system is simulated in Simulink platform(6.2). The solver used is ode45 (Dormant Prince) with variable step size.

The simulink implementation of the heart model is taken from [6].

6.4 Results

The pressure waveforms in left ventricle, left atrium, aorta and arm as well as the volume in left ventricle are plotted(6.3).

We see that the simulated waveforms are similar to the actual waveforms. The shape of the pressure wave in the arm is qualitatively similar to the in vivo waveform to the extend that the incisura is damped.

There is a significant quantitative error in the pressure waveform in the arm. This might have been caused due to the mismatch between the two models during

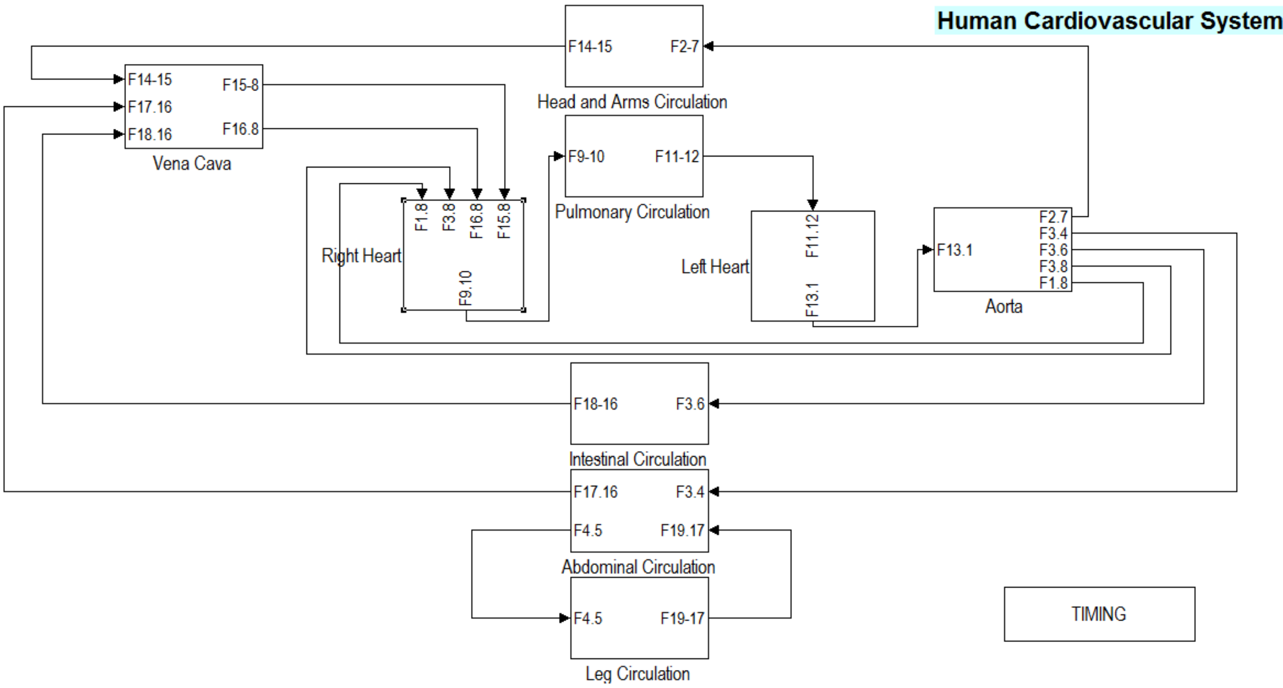

FIGURE 6.2: Simulink Model of Cardiovascular System

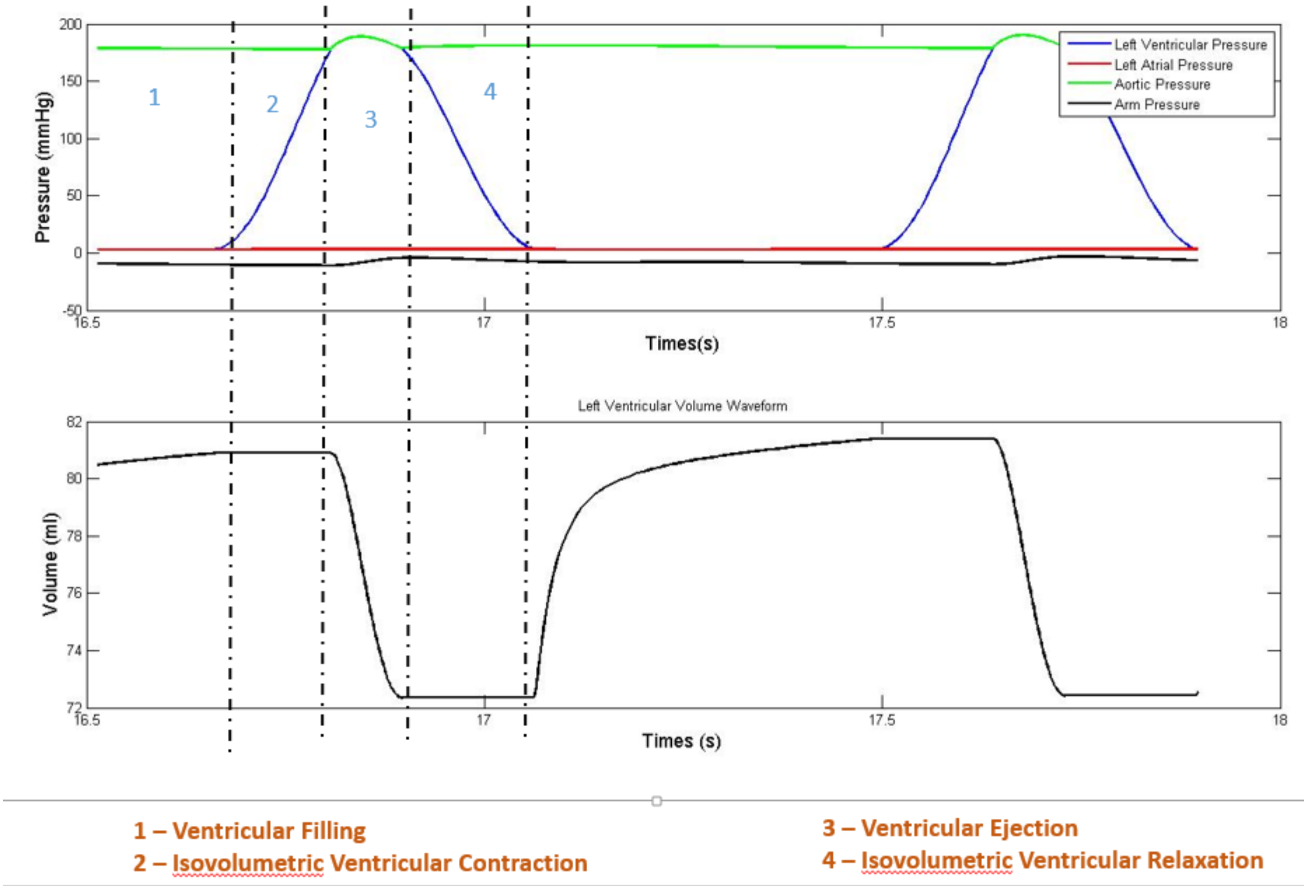

FIGURE 6.3: LA, LV, Aorta and unnormalized Arm Pressure Waveforms

integration. To account this error the pressure waveform at the arm has been normalized by shifting and scaling to a certain factor. The resulting waveform is given below(6.4).

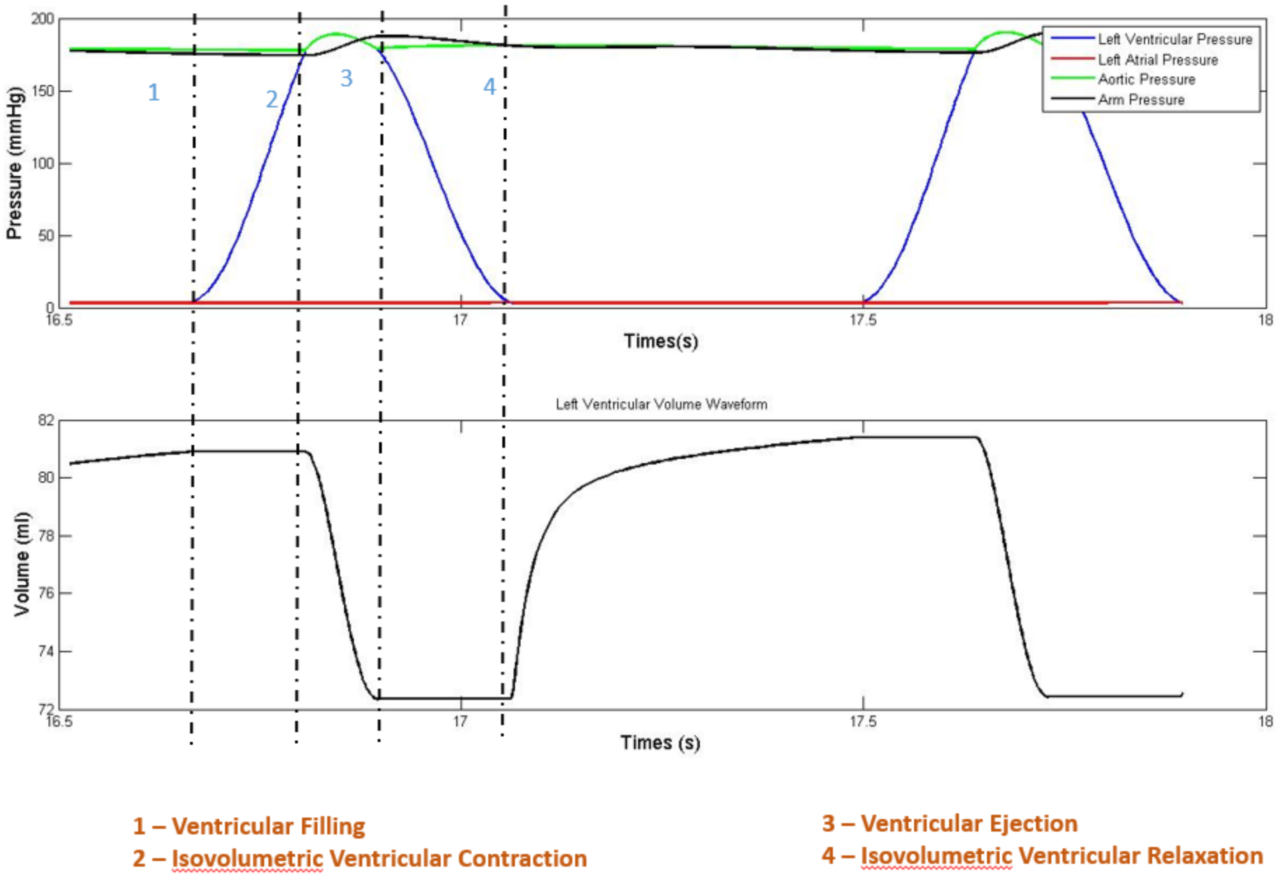

FIGURE 6.4: LA, LV, Aorta and normalized Arm Pressure Waveforms

CHAPTER 7

CONCLUSION

7.1 Conclusion

A study of ancient pulse diagnosis is carried out. It is understood that a pulse diagnosis measurement system is a simple and cost effective method to get accurate diagnosis about the diseases in the human body. This work is part of a larger work of developing such a system. Here, the objective is to understand the genesis of three pulses in the radial artery in the light of modern medical science. Two existing models of the human cardiovascular system has been studied. These models doesn't shed light into the three pulse concept in Nadipariksha. An integrated model of the two models has been developed which is in the dierection of explaining the three pulse concept.

Using the combined model one pressure waveform at the arm has been generated. With further investigation, a model could be developed from the combined model which would give results with which the three pulses at the radial artery can be generated accurately.

7.2 Future Work

In this work, only a single pressure waveform corresponding to head and arm can be generated. In future the head and arm segment could be divided into smaller segments such that separate pressure waveform at the radial artery can be generated. Also attempts should be made to improve the accuracy of the CVS representation. A CVS model with the following accounted would be a more accurate representation of the system.

- Consider the nonlinearlities in the system.
- Account for reflections of waves at arterial junctions.
- Include the effects of blood being non-Newtonian.
- Include the baroreflex control in the CVS.
- Model nerve control should be included.

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